

### **REMARKS/ARGUMENTS**

Claims 1-62 are pending in the captioned application. Claims 57-62 have been withdrawn as drawn to a non-elected invention, while claims 1-56 stand rejected. Applicants have amended claim 1. Applicants respectfully submit that the amendments are fairly based on the specification and respectfully request their entry. Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

The Examiner has rejected claims 1-7, 9, 11-13, 15-18, 20, 30-38, 40, 42-45, 47, 55 and 56 under 35 U.S.C. § 102(b). These claims are rejected as being anticipated by Williams et al. (WO 2001/94609). This rejection is respectfully traversed.

As the Examiner points out, Williams et al. discloses a method for solid phase sequencing of a nucleic acid, which method includes the use of a labeled NP having a detectable moiety, wherein the detectable moiety is released as a charged detectable moiety when the NP is incorporated into the primer. After the application of an energy field, the charged detectable moiety is detected thereby the target nucleic acid sequenced (see e.g. page 4, lines 20-29). Williams et al. teaches that the NP is a nucleoside triphosphate, and the detectable moiety is a gamma-phosphate with a fluorophore attached (see e.g. page 4, lines 14-15). Williams et al. teaches that a phosphatase can be used to enhance “the charge-switch magnitude by dephosphorylating the P<sub>Pi</sub>-F” (see e.g. page 25, lines 12-13).

The sequencing method of instant claim 1 includes the use of a terminal-phosphate-labeled nucleoside polyphosphate. However, the label on the terminal phosphate is a phosphatase activatable label (page 19, lines 12-13). Moreover, the labeled polyphosphate produced from the polymerase reaction is treated with a phosphatase to generate a detectable species that is readily distinguishable from the labeled polyphosphate or the terminal-phosphate-labeled nucleoside polyphosphate (page 4, lines 6-9; page 12, lines 20-23; page 19, lines 12-22; Table 1). This detectable species is subsequently detected. Applicants have amended claim 1 to further clarify these points.

Applicants respectfully submit that while Williams et al. suggests the use of a phosphatase to enhance the charge-switch magnitude of the labeled polyphosphate, the reference does not teach the use of a nucleoside polyphosphate containing a phosphatase activatable label. In fact, the property/detectability of the label in Williams et al. remains the same before and after phosphatase treatment. The only change phosphatase treatment brings to the label in Williams et al. is a change in charge. In comparison, in claim 1 of the instant application, a detectable species is generated after phosphatase treatment (e.g., phosphatase activatable) and is readily distinguishable from the labeled polyphosphate. Applicants assert that this is not taught by Williams et al.

Applicants submit that Williams et al. requires a separation by charge of the dye-labeled pyrophosphate product of the polymerase reaction (or the phosphatase treated product, with enhanced charge-switch magnitude) from the dye-labeled nucleotides, prior to detection of the dye (see e.g. Figure 7). This is critical for Williams et al., as the

detectable property of the dye after phosphatase treatment is the same as prior to the treatment. Without physical separation, it is impossible to distinguish the reaction product from the dye-labeled nucleotide. In claim 1 of the current invention, however, because the detectable species generated by phosphatase treatment is readily distinguishable from untreated labeled polyphosphate, or labeled nucleotide, a separation of the dye product (detectable species) is not necessary. In fact, the labeled nucleotide in the current application is inert to phosphatase treatment, and therefore, phosphatase treatment can be carried out simultaneously with the polymerase reaction (see e.g. page 3, lines 17-31; claim 13).

Applicants submit that there is no teaching or suggestion in Williams et al. for a sequencing method represented by claim 1 of the instant application. As such, Applicants submit that the § 102(b) rejection of claim 1 over Williams et al., and dependent claims 9, 11-13, 15-18, 20 and 30-31 can not be sustained and should be withdrawn.

With regard to claim 32 and the claims dependent thereupon (claims 33-56), Applicants respectfully submit that these claims relate to a solid phase sequencing method, which method includes a terminal-phosphate-labeled nucleotide polyphosphate with 4 or more phosphates (see e.g. lines 5-6 of claim 32). Applicants submit that this limitation is not found in Williams et al. Therefore, claim 32 and related dependent claims should be allowable. Applicants respectfully submit that the § 102(a) rejections to claim 32 and dependent claims 33-38, 40, 42-45, 47 and 55-56 should be withdrawn.

The Examiner has rejected claims 8 and 39 under 35 U.S.C. § 103(a), as being unpatentable over Williams et al. in view of Wittwer et al. (US 6,174,670). This rejection is respectfully traversed. As stated above, Williams et al. does not disclose or even suggest the independent claims 1 and 32, upon which claims 8 and 39 depend, respectively. In view of this, Applicants submit that the § 103(a) rejections over Williams et al. in view of Wittwer et al. should also be withdrawn.

The Examiner has rejected claims 10 and 41 under 35 U.S.C. § 103(a), as being unpatentable over Williams et al. in view of Keller et al. (US 5,656,462). This rejection is respectfully traversed. As stated above, Williams et al. does not disclose or even suggest the independent claims 1 and 32, upon which claims 10 and 41 depend, respectively. In view of this, Applicants submit that the § 103(a) rejections over Williams et al. in view of Keller et al. should also be withdrawn.

The Examiner has rejected claims 19 and 46 under 35 U.S.C. § 103(a), as being unpatentable over Williams et al. in view of Lichtenwalter et al. (US 5,683,875). This rejection is respectfully traversed. As stated above, Williams et al. does not disclose or even suggest the independent claims 1 and 32, upon which claims 19 and 46 depend, respectively. In view of this, Applicants submit that the § 103(a) rejection over Williams et al. in view of Lichtenwalter et al. should also be withdrawn.

The Examiner has provisionally rejected claims 1-5, 9-12, 16-18, 20, 30-36, 40-45, 47, 55 and 56 under “obviousness-type double patenting as being unpatentable over claims 1, 2, 3, 12, 14, 16, 17, 25 of copending Application No. 11/255683.” In response,

Applicants submit concurrently herewith a Terminal Disclaimer, terminally disclaiming the term of any patent issuing on the instant application over the term of co-pending application number 11/255,683. Applicants respectfully assert that this Terminal Disclaimer overcomes the Examiner's grounds for rejection.

The Examiner has provisionally rejected claims 1-6, 9, 11-37, 38, 40, 42, 44, 45 and 47-56 under "obviousness-type double patenting as being unpatentable over claims 6-8, 10-12, 15-22, 25, 28, 29 of U.S. Patent No. 7,041,812 in view of Williams et al (WO/2001/94609)." In response, Applicants submit concurrently herewith a Terminal Disclaimer, terminally disclaiming the term of U.S. Patent No. 7,041,812. Applicants respectfully assert that this Terminal Disclaimer overcomes the Examiner's grounds for rejection.

The Examiner has provisionally rejected claims 1-6, 9-34, 38, 40-45, 47-49 and 52-56 under "obviousness-type double patenting as being unpatentable over claims 1-4, 6-10, 12-14, 16-19, 21-24, 26, 44-46, 67-68 of U.S. Patent No. 7,052,839 in view of Williams et al (WO/2001/94609)." In response, Applicants submit concurrently herewith a Terminal Disclaimer, terminally disclaiming the term of U.S. Patent No. 7,052,839. Applicants respectfully assert that this Terminal Disclaimer overcomes the Examiner's grounds for rejection.

The Examiner has provisionally rejected claims 1-6, 9-18, 20-38, 40-46, 48, 49 and 52-56 under "obviousness-type double patenting as being unpatentable over claims 1, 4, 19, 22-30, 35-37, 39-40 of U.S. Patent No. 7,033,762 in view of Williams et al

(WO/2001/94609).” In response, Applicants submit concurrently herewith a Terminal Disclaimer, terminally disclaiming the term of U.S. Patent No. 7,033,762. Applicants respectfully assert that this Terminal Disclaimer overcomes the Examiner’s grounds for rejection.

The Examiner has provisionally rejected claims 1-6, 9, 10, 12-34, 38, 40-43, 47-49 and 55-56 under “obviousness-type double patenting as being unpatentable over claims 1-3, 6, 7, 12-21, 23, 26, 27, 30, 34, 36, 40, 43, 44, 46, 47, 49, 56-58 of copending Application No. 10/113030 in view of Williams et al (WO/2001/94609).” In response, Applicants submit that 10/113,030 is now U.S. Patent No. 7,052,839, and submit concurrently herewith a Terminal Disclaimer, terminally disclaiming the term of U.S. Patent No. 7,052,839. Applicants respectfully assert that this Terminal Disclaimer overcomes the Examiner’s grounds for rejection.

The Examiner has provisionally rejected claims 1-6, 9-16, 20-38, 40-45, 47-49 and 55-56 under “obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 6, 12, 15, 17-20, 22, 25, 26, 28-30, 34, 40, 58, 64 of copending Application No. 10/113025 in view of Williams et al (WO/2001/94609).” In response, Applicants submit that 10/113,025 is now U.S. Patent No. 7,033,762 and submit concurrently herewith a Terminal Disclaimer, terminally disclaiming the term of U.S. Patent No. 7,033,762. Applicants respectfully assert that this Terminal Disclaimer overcomes the Examiner’s grounds for rejection.

The Examiner has provisionally rejected claims 1-6, 9-16, 20-26, 31-33, 36-45, 47-49 and 55-56 under “obviousness-type double patenting as being unpatentable over claim 1, 3, 4, 12-14, 18-24, 26-28, 30, 32, 34 of copending Application No. 10/651362 in view of Williams et al (WO/2001/94609).” In response, Applicants submit that 10/651,362 is now U.S. Patent No. 7,125,671 and submit concurrently herewith a Terminal Disclaimer, terminally disclaiming the term of U.S. Patent No. 7,125,671. Applicants respectfully assert that this Terminal Disclaimer overcomes the Examiner’s grounds for rejection.

The Examiner has provisionally rejected claims 1-6, 9-16, 20-26, 30-34, 36-38, 40, 41-45, 47-49 and 55-56 under “obviousness-type double patenting as being unpatentable over claims 1, 4, 6, 9, 11, 15, 16, 17, 18, 21, 23, 26, 27, 28, 29, 30 and 36 of copending Application No. 10/651582 in view of Williams et al (WO/2001/94609).” In response, Applicants submit concurrently herewith a Terminal Disclaimer, terminally disclaiming the terms of any patent issuing on the instant application over the term of copending application number 10/651,582. Applicants respectfully assert that this Terminal Disclaimer overcomes the Examiner’s grounds for rejection.

The Examiner has provisionally rejected claims 8 and 39 under obviousness-type double patenting as being unpatentable over, in the alternative claims 15 and 22 of ‘812, 1 of ‘839, 22 of ‘762, 1, 2, 26, 27 of ‘030, 3 and 26 of ‘025, 24 of ‘362, 1 and 4 of ‘582, and Williams et al., each further in view of Wittwer et al. (US 6,174,670). In response, Applicants submit that concurrently a Terminal Disclaimer is submitted for each of co-

owned patents/applications, terminally disclaiming the terms of any patent issuing on the instant application over the term of patents/co-pending applications at issue. Applicants respectfully assert that these Terminal Disclaimers overcome the Examiner's grounds for rejection.

The Examiner has provisionally rejected claims 19 and 46 under obviousness-type double patenting as being unpatentable over, in the alternative claims 15 and 22 of '812, 1 of '839, 22 of '762, 1, 2, 26, 27 of '030, 3 and 26 of '025, 24 of '362, 1 and 4 of '582, and Williams et al., each further in view of Wittwer et al. (US 6,174,670). In response, Applicants submit that concurrently a Terminal Disclaimer is submitted for each of co-owned patents/applications, terminally disclaiming the terms of any patent issuing on the instant application over the term of patents/co-pending applications at issue. Applicants respectfully assert that these Terminal Disclaimers overcome the Examiner's grounds for rejection.

Applicants respectfully assert that the claims are in allowable form and earnestly solicit the allowance of claims 1-56.



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Reply to Office action of October 12, 2006

Early and favorable consideration is respectfully requested.

Respectfully submitted,

GE Healthcare Bio-Sciences Corp.



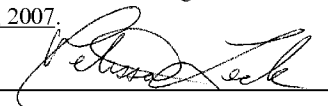
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